



Human Research Program Bed Rest Experiment Information Package

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**Flight Analogs Project
Human Research Program**

HRP Bed Rest Experiment Information Package

Descriptions of standard services provided in this document reflect what is currently being done for the bed rest project at the NASA Flight Analogs Research Unit. Standard measures have undergone an annual review and the Flight Analogs project is in the process of making changes to these measures. Please use this document as a general guide to the standard measures for the purpose of preparing research protocols. Questions related to this document can be directed to:

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NASA FLIGHT ANALOGS PROJECT STANDARD SERVICES

The NASA Flight Analogs Project (FAP) provides a forum for investigating the effects of hypogravity on the physiology of the whole body. The information provided in this document describes the standardized conditions, data collection, and services for 90-day six degrees head down bed rest studies performed in the Flight Analogs Research Unit of the General Clinical Research Center located at the University of Texas Medical Branch in Galveston, TX. NASA is developing a lunar analog with standardized conditions, data collection, and services that are expected to be similar to those described here. Standardized study plans are integrated with investigator protocols on a non-interference basis.

1.0 NASA FLIGHT ANALOGS PROJECT

- Provides a set of standardized bed rest study conditions so results may be compared and contrasted
- Collects a set of Standard Measures for every bed rest subject
- Maximizes resources by combining individual investigations into integrated studies

2.0 BED REST STANDARDIZED CONDITIONS

- Duration: 90 days
- Bed Position: 6 degrees head down tilt, continuous for the duration of the study
- Environmental: 70-74 degrees F.
- Light/Dark Cycle: Lights on 0600, lights out 2200 (no napping)
- Daily Measurements:
 - Blood Pressure, Heart Rate, Respiratory Rate, Temperature
 - Body Weight
 - Fluid Intake and Output
- Monitoring: By Subject Monitors in person or via in room camera 24 hours a day
- Stretching Regimen: Twice daily
- Physiotherapy: Every other day during bed rest and every day for the first seven days post bed rest

3.0 BED REST STANDARDIZED DIET

- Isocaloric diet based on the NASA space flight nutritional requirements
- Carbohydrate:Fat:Protein ratio – 55:30:15
- Fluid intake of 28.5 ml/kg body wt (2000 ml/70 kg subject)
- No caffeine, cocoa, chocolate, tea or herbal beverages
- All food must be consumed
- Caloric intake adjusted to maintain weight within 3% of day 3 of head down tilt
- Iron supplementation is provided for all female subjects
- Iron supplementation is provided for male subjects with a low ferritin at study entry

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Nutrient	Bed Rest Recommendation	Flight Recommendation
Energy, kcal	Maintain BW	WHO (moderate activity)
Protein, g	12-15% of total energy	12-15% of total energy
% kcal from fat	30-35% of total energy	30-35% of total energy
% kcal from protein	12-15% of total energy	12-15% of total energy
Vitamin A, µg RE	1000 µg RE	1000 µg RE
Vitamin D, µg RE	10 µg RE (400 IU)	10 µg RE (400 IU)
Vitamin E, mg α-TE	20 mg α-TE	20 mg α-TE
Vitamin K, µg	80 µg (M), 65µg (F)	80 µg (M) 65µg (F)
Vitamin C, mg	100 mg	100 mg
Thiamin, mg	1.5 mg	1.5 mg
Riboflavin, mg	2.0 mg	2.0 mg
Niacin, mg	20 mg	20 mg
Pantothenic acid, mg	5.0 mg	5.0 mg
Vitamin B6, mg	2.0 mg	2.0 mg
Folate, µg	400 µg	400 µg
Vitamin B12, µg	2.0 µg	2.0 µg
Calcium, mg	1000 – 1200 mg	1000 – 1200 mg
Phosphorus, mg	1000 – 1200 mg	1000 – 1200 mg
Magnesium, mg	350 mg (M), 280 mg (F)	350 mg (M) 280 mg (F)
Iron, mg	10 mg (M), 18 mg (F)	10 mg
Zinc, mg	15 mg	15 mg
Copper, mg	1.5-3.0 mg	1.5-3.0 mg
Selenium, µg	70 µg	70 µg
Sodium, mg	<3500 mg	<3500 mg
Potassium, mg	3500 mg	3500 mg
Fiber, g	10-25 g	10-25 g
Manganese, mg	2.0-5.0 mg	2.0-5.0 mg

Figure 1: Bed Rest Nutrition Intake Recommendations

4.0 BED REST STANDARD MEASURES

BACKGROUND

An overview of the standard measures to be performed during all flight analog/bed rest studies is presented here. Standard measures provide a description of the physiologic responses to bed rest in humans across disciplines. These protocols are performed at the General Clinical Research Center and are integrated with science investigation requirements on a non-interfering basis. The standard measures can be utilized to describe gender differences in the physiological responses to bed rest, provide a basis for comparisons of bed rest results with results from flight investigations, and provide ancillary data to individual investigators. A schedule of the standard measures is located after the descriptions.

NASA FLIGHT ANALOGS PROJECT

STANDARD SERVICES

NEUROCOGNITIVE ASSESSMENT (WinSCAT)

Cognitive function of all subjects will be measured using the same neurocognitive assessment tool required for crewmembers on long-duration space flight missions. This lap-top based activity obtains objective measures of cognition before, during and after exposure to long-duration bed rest to assess the cognitive effects of simulated microgravity induced by 6 degree head down tilt. The five cognitive subtests are Coding Memory - Learning, Continuous Processing Task, Match to Sample, Mathematics, and Coding Delayed Recall. These tests measure sustained concentration, verbal working memory, attention, short-term memory testing, spatial processing, and math skills. The test usually takes 11-15 minutes to complete.

BONE MINERAL DENSITY (DXA)

Dual Energy X-Ray Absorptiometry will be used to obtain measures of bone mineral density. A Hologic Discovery whole body densitometer will be used to perform scans, and scan analyses will be performed using the software provided by Hologic. Bone mineral density will be determined for the whole body and for regional bone sites at both hips, lumbar spine, calcaneus, and forearm. All six scans are performed in triplicate.

	EDE (Men)	EDE (Pre-menopausal Women)
Whole body	2.34 mR	3.06 mR
Hip (R and L)	0.72 mR	6.60 mR
Lumbar Spine	1.20 mR	1.20 mR
Calcaneus	0.03 mR	0.03 mR
Forearm	0.03 mR	0.03 mR
Total	4.32 mR	10.92 mR

Figure 2. Associated Radiation Exposure Per Session for Triplicate Scans

PERIPHERAL QUANTITATIVE COMPUTERIZED TOMOGRAPHY (pQCT)

A Stratec XCT 3000 scanner will be used to provide measures of bone mass and structure to be used in estimating bone strength. The scanning positions will be measured from the endplate of the tibia and will be at the 4%, 14%, 33%, and 66% positions and also the proximal tibia at the patella insertion. Each slice has a nominal thickness of 2.5 mm. The radiation exposure is approximately 1.5 mR per session.

Scan analyses will be performed using the analysis software provided by the manufacturer. From each scan several parameters will be measured: trabecular area and density, cortical area and density, bone mineral content, and a “strength-strain index” (SSI), which is a density weighted section modulus.

CLINICAL NUTRITIONAL ASSESSMENT

General blood and urine chemistry, electrolytes, selected markers of hematological, protein, vitamin and mineral status, markers of oxidative damage, and markers of bone metabolism will be assessed. In addition, cellular mineral content (Sodium, Potassium, Chloride, Calcium,

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Phosphorous, Magnesium) will be analyzed from sublingual epithelial cells collected with a wooden spatula by scraping the floor of the mouth.

Serum Measurements for Nutrition Standard Measure

Chemistry

Sodium, Potassium, Chloride, Creatinine, Aspartate Transaminase (AST), Alanine Transaminase (ALT), Cholesterol, Triglyceride

Portable Clinical Blood Analyzer

Hemoglobin, Hematocrit, Ph, Ionized Calcium, Potassium, Sodium, Glucose

Mineral Status

Zinc, Selenium, Iodine, Copper, Ceruloplasmin

Calcium and Bone Metabolism Markers

25-Hydroxyvitamin D, 1, 25-Dihydroxyvitamin D, Intact Parathyroid Hormone (PTH), Osteocalcin, Alkaline Phosphatase, Bone Specific Alkaline Phosphatase (BSAP), Serum Calcium, C-telopeptide (CTX), Helical Peptide (HP), Osteoprotegerin (OPG), Osteoprotegerin ligand (receptor activator of nuclear factor- κ B ligand or RANKL), Insulin-like Growth Factor, Leptin

Hematologic and Iron Status Indicators

Hemoglobin, Hematocrit, Mean Corpuscular Volume (MCV), Transferrin Receptors, Transferrin, Ferritin, Ferritin Iron, Ferritin Iron % Saturation, Folate, RBC, Iron

Protein Status

Retinol Binding Protein, Transthyretin, Total Protein, Albumin, Alpha 1 globulin, Alpha 2 globulin, Beta globulin, Gamma globulin

Hormones

Testosterone, Estradiol, Dehydroepiandrosterone (DHEA), Dehydroepiandrosterone Sulfate (DHEA-S), Cortisol

Water Soluble Vitamin Status

Erythrocyte Transketolase Stimulation, Erythrocyte Glutathione Reductase Activity, Erythrocyte nicotinamide adenosine dinucleotide and nicotinamide adenosine dinucleotide phosphate (NAD/NADP), Erythrocyte Transaminase Activity, Red Cell Folate, Folate, Homocysteine, Vitamin C, Pyridoxal 5-phosphate (PLP)

Fat Soluble Vitamin Status

Retinol, Retinyl palmitate, β -carotene, α -carotene, Serum Phylloquinone, α -tocopherol, γ -tocopherol, Tocopherol : lipid ratio

Antioxidants and Markers of Oxidative Damage

Total Antioxidant Capacity (TAC), Superoxide Dismutase (SOD), Glutathione Peroxidase (GPX), Malondialdehyde (MDA), 4-OH-alkenal, 4-hydroxynonenal, Glutathione Protein Carbonyls, Prostaglandin F₂- α (PG F₂- α)

Urinary Measurements for Nutrition Standard Measure

General

Total volume, pH, Creatinine

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Bone Metabolism Markers

N-telopeptide (NTX), Pyridinoline (PYD), Deoxypyridinoline (DPD), γ -carboxy glutamic acid

Minerals

Calcium, Phosphorus, Magnesium, Copper, Selenium, Zinc, Iodine

Water Sol. Vitamins

N-methyl nicotinamide, 2-pyridone, 4-pyridoxic acid

Protein Status

3-methyl histidine

Antioxidants

8-OH deoxyguanosine

Renal Stone Risk

Sodium, Potassium, Uric Acid, Citrate, Oxalate, Sulfate, Supersaturation of Calcium Oxalate, Brushite, Struvite, Sodium, Urate, Uric Acid

CLINICAL LABORATORY ASSESSMENT

Additional blood and urine studies will be performed to monitor subject health status and provide additional data.

Serum Measurements for Clinical Laboratory Standard Measure

Chemistry Profile

Carbon Dioxide, Blood Urea Nitrogen, Phosphorous, Magnesium, Bilirubin, Glutamyltransferase, Alkaline Phosphatase, Lactate Dehydrogenase, Creatine Kinase, Uric Acid, C Reactive Protein (hs CRP)

CBC/differential/platelets

White Blood Count and differential, Red Blood Count, Hemoglobin, Hematocrit, Mean Corpuscular Volume, Mean Corpuscular Hemoglobin (MCH), Mean Corpuscular Hemoglobin Concentration (MCHC), Relative (Red Cell) Distributive Width (RDW), Platelet Count, Reticulocyte Count

Iron Profile

Iron, Total Iron Binding Capacity (TIBC), Transferrin, Transferrin Saturation, Ferritin

Ionized Calcium Profile

Serum Ionized Calcium, pH-Serum, Ionized Calcium at pH 7.40

Hormones

Thyroxine (Free T4), Thyroid Stimulating Hormone (hTSH III)

Urinary Measurements for Clinical Laboratory Standard Measure

Urinalysis

Specific Gravity, pH, Color, Appearance, Protein, Glucose, Bilirubin, Urobilinogen, Ketone, Nitrite, Blood, Leukocyte Esterase,

Other

Creatinine

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ISOKINETIC MUSCLE FUNCTION TESTING

Isokinetic muscle strength and endurance tests will be conducted prior to and following bed rest. Muscle performance testing will be administered using a standard clinical isokinetic dynamometer (Cybex NORM) on selected muscle groups. A standard protocol for warm-up prior to testing will be followed for each muscle group. Testing will be performed on the right limb. The protocol will be performed as described below:

Warm-up	5 minutes at 50 Watts on upright cycle ergometer
Knee Flexion/ Extension (Seated):	<ul style="list-style-type: none"> • Position Subject • Set Range of Motion (20-95 degrees) • 5 submaximal concentric repetitions at 60 deg/sec: extension and flexion • 5 concentric maximal reps at 60 deg/sec: extension • 5 concentric maximal reps at 60 deg/sec: flexion • 2-3 submaximal concentric repetitions at 180 deg/sec: extension and flexion • Endurance test: 20+1 reps. at 180 deg/sec (extension and flexion)
Ankle Plantar/Dorsiflexion (Prone):	<ul style="list-style-type: none"> • Position Subject • Set Range of Motion (minimally -15 to +30 degrees) • 5 submaximal concentric repetitions at 30 deg/sec: extension and flexion • 5 concentric maximal reps at 30 deg/sec: plantar flexion • 5 concentric maximal reps at 30 deg/sec: dorsiflexion • 2-3 submaximal eccentric repetitions at 30 deg/sec: extension and flexion • 5 eccentric maximal reps at 30 deg/sec: plantar flexion • 5 eccentric maximal reps at 30 deg/sec: dorsiflexion
Trunk Extension/Flexion (Standing)	<ul style="list-style-type: none"> • Position Subject • Set Range of Motion (0-90 degrees) • 5 submaximal concentric repetitions at 30 deg/sec: extension and flexion • 5 concentric maximal reps at 60 deg/sec: extension • 5 concentric maximal reps at 60 deg/sec: flexion

Figure 3. Isokinetic Protocol

AEROBIC CAPACITY – CYCLE ERGOMETRY

To assess cardiovascular functional performance, maximum aerobic capacity will be measured in each subject using a graded cycle exercise test. Subjects will pedal a cycle ergometer at increasing work loads (50-350 Watts) while heart rate, blood pressure, and oxygen uptake are monitored. Exercise tests will be conducted prior to bed rest and following bed rest. These tests will be performed on a cycle ergometer (LODE™ Excalibur Sport) with the subject in the upright (seated) position. Testing will be the standard NASA test used to determine peak cycle heart rate (HR) and oxygen consumption (Parvomedics™ TrueOne system). Details of the test protocols are shown below.

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Protocol A		Protocol B	
Work Rate (Watts)	Time (min)	Work Rate (Watts)	Time (min)
50	3	50	3
100	3	75	3
150	3	100	3
175	1	125	1
200	1	150	1
225	1	175	1
250	1	200	1
+25*	+1*	+25*	+1*

Figure 4. Cycle Ergometer Exercise Protocols^a for Determination of Peak $\dot{V}O_2$.

- * Test continues until subject reaches peak effort. Peak effort is verified as: (1) Plateau in $\dot{V}O_2$ despite a work rate increase, or (2) Attainment of HR > 90% age-predicted maximum accompanied by a respiratory exchange ratio ($\dot{V}CO_2 / \dot{V}O_2$) of greater than 1.10.
- ^a Protocol A is used for subjects weighing > 65 kg. Some discretion is used for the assignment of protocols. For example, Protocol A is also appropriate for a 62 kg individual who regularly performs cycle exercise.

FUNCTIONAL FITNESS

The Functional Fitness Test is used by the Astronaut Strength Conditioning and Rehabilitation team (ASCR) to establish baseline muscle strength, endurance, and flexibility before space flight and to monitor their rehabilitation after long duration missions. Data from bed rest subjects will provide a comparison of bed rest to space flight and a tool for monitoring test subject rehabilitation. Free weight muscle strength and endurance tests are functional strength measurements because they are closely associated with activities of daily living (ADL), such as standing up from a chair or bending to lift a box which involves production of force to overcome the inertia of the body mass as well as the inertia of the external object lifted. Additionally, ADL's are multi-joint and multi-muscle activities. Before and after bed rest, subjects will perform two 1-repetition maximum (1-RM) tests on a Cybex™ leg press machine. Subjects will warm up with 5 minutes on a cycle ergometer at 50 to 100 watts. After cycling, the subjects will execute a stretching routine followed by a ramp-up procedure on the leg press: 1x8 (50% projected 1-RM), 1x5 (60% projected 1-RM), 1x3 (70% projected 1-RM), 1x1 (80% projected 1-RM), 1x1 (90% projected 1-RM), and 1x1 (100% of projected 1-RM). Subjects will continue to perform 1 repetition with weight increasing by 3% to 5% until failure. They will be given a 2 to 5-minute rest between sets. The maximum amount lifted will be recorded and documented as the subject's 1-RM. In addition to free weight muscle strength, subjects will perform a 2 minute push up and sliding crunch test to measure local muscle endurance according to the guidelines outlined by the United States Military. They will also perform a pull up test to failure to measure

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muscle endurance/ strength, and a sit and reach test to measure lower back and hamstring flexibility.

FUNCTIONAL NEUROLOGICAL ASSESSMENT (POSTURE)

Sensory-motor balance control function will be tested before and after bed rest using a NeuroCom Equitest Posturography System (Clackamas, OR) and protocol similar to that used on many short duration space flight crewmembers and currently required for all returning long-duration crew members. During these sessions, the subject stands on a movable, force-sensing, support surface and within a movable visual enclosure. Movements of the support surface and/or visual enclosure, under precise control of a computer, are used to modify the sensory conditions and/or to impose unexpected perturbations. The Sensory Organization Tests (SOT) assess the subject's ability to make effective use of visual, vestibular, and somatosensory information for maintaining upright stance. During some trials, the support surface and/or visual surround are moved in relation to the subject's sway, referred to as sway-referencing. Postural sway is measured during 20-s trials, including combinations of somatosensory conditions (fixed-support, sway-referenced support) and visual conditions (eyes open, eyes closed, sway-referenced vision). The primary outcome variable is the Equilibrium (EQ) score derived from the subject's peak-to-peak antero-posterior (AP) sway during each trial relative to a theoretical stability limit of 12.5 degrees. Postural performance will then be repeated during active head tilts with eyes closed and a fixed-support or sway-referenced support surface. Head movements will be made in the pitch plane to $\pm 20^\circ$, paced by a sinusoidal auditory tone at 0.33Hz. The velocity of head movements and other body segments are monitored with an Optotrak motion analysis system to determine the type of strategy the subject was using to maintain balance. The subjects will also be challenged by sudden base-of-support perturbations (toes-up rotations of 10° displacement over 500 ms elapsed time). Twelve perturbations will be presented sequentially with randomly varied 10-15 s intervals between and randomly varied visual input (6 trials with eyes open and 6 with eyes closed). Post-bed rest testing will be discontinued after pre-bed rest performance levels have been achieved on two consecutive test sessions.

CARDIOVASCULAR ASSESSMENT

Neuroendocrine and Cardiovascular Responses to Tilt

Although a 10-minute tilt test (at 80 degrees head-up tilt) is a component of the current ISS medical assessment testing, it is not adequate to truly evaluate orthostatic tolerance. This is due to the very limited time constraints on landing day and to the limited amount of blood that can be sampled from long-duration astronauts. Therefore, during bed rest an enhanced tilt test is done to gain additional information and to better evaluate mechanisms of possible countermeasures. Subjects will be placed on the tilt table, and blood drawn for measurement of neuroendocrine parameters. The subject will then be tilted upright at 80 degrees for 30 minutes. Then a final sample will be drawn for a repeat of the supine blood measurements. If the subject cannot tolerate 30 minutes of upright tilt, the tilt table will be placed in the supine position and the blood drawn immediately.

Blood Volume

Blood volume will be measured using the carbon monoxide re-breathing technique.

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Cardiac Function

The purpose of the cardiac function measures is to collect a definitive set of measurements of changes in cardiac function during bed rest. Echocardiography will be performed on bed-rest subjects utilizing views consistent with standards established by the American Society of Echocardiography.

Hemodynamic assessment will be obtained by use of continuous, pulsed wave and color flow Doppler. All four cardiac valves will be evaluated for regurgitation. Velocity measurement of tricuspid regurgitation, if present, provides an accurate measurement of the pressure difference between the right ventricle and right atrium and leads to an estimation of peak pulmonary pressure. The acceleration time of flow through the pulmonary artery can also give an estimation of pulmonary pressure.

To address diastolic function, several traditional echocardiographic measurements and indices (including mitral E and A wave velocities, mitral deceleration time and isovolumic relaxation time) will be employed in addition to more investigational measures.

Many of the same parameters acquired during supine rest are also to be acquired during upright tilt after the subject has been upright for over one minute. Not only will this address the above cardiac parameters under differing loading conditions; but the difference between the supine and upright values can offer an insight into the ability of the heart and cardiovascular system to adapt to a stress following bed rest. The measurements included during tilt include Doppler evaluation of the mitral, tricuspid and aortic valves in addition to tissue Doppler of the lateral annuli of the mitral and tricuspid valves and color M-mode flow propagation velocity. Two and three dimensional imaging of the heart also allows for subsequent volume measurement.

IMMUNE FUNCTION ASSESSMENT

General Immune Status

A general immune assessment will be performed, consisting of white blood cell count and differential, immunophenotype distribution, T cell function, and intracellular cytokine profiles. Regarding immunophenotype, the following peripheral leukocyte populations will be assessed: leukocyte differential, lymphocyte subsets, T cell subsets, T cell subset memory/naïve ratio, levels of peripheral activated T cells. For T cell function, whole blood cultures will be pulsed with mitogenic stimuli, following which T cell expression of activation markers will be assessed. Intracellular cytokine profiles consist of IFN γ and IL-2 expression T cell subsets following PMA+ionomycin stimulation in the presence of monensin to allow intracellular accumulation.

The phenotypic analysis of leukocyte subpopulations will be performed to correlate with the results from the WBC and differential hematology data. The antibody combinations for immunophenotype and functional analysis by flow cytometry are as follows:

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LEUKOCYTE SUBPOPULATION DISTRIBUTION

FITC	PE	ECD	PercP	CELL POPULATIONS ASSESSED
CD14	CD19		CD45	WBC Differential/B-cells
CD3	CD56		CD45	Lymphocytes subsets
CD4	CD8		CD3	T cell subsets
CD45RA	CD45RO	CD8	CD3	T cell subsets; memory/naïve T cell subsets
HLA-DR	CD69	CD8	CD3	Early, late activated T cell subsets

CYTOKINE PRODUCTION PROFILES

FITC	PE	ECD	PercP	
IL-2	IFN γ	CD8	CD3	T cell cytokine profiles

T CELL FUNCTION (24 hr ctl, A+B, 3/28)

FITC	PE	ECD	PercP	
CD25	CD69	CD8	CD3/4	Culture activated T cell responses.

Figure 5. Antibody Combinations for Immunophenotype and Functional Analysis by Flow Cytometry

Viral-Specific Immunity

For characterization of virus-specific T-cells, flow cytometric assays (tetramer staining and intracellular cytokine staining) for virus EBV-specific T-cells will be performed.

Latent Viral Reactivation

Standard techniques (immunofluorescence assay) will be used on serum/plasma specimens for determining Immunoglobulin (Ig)G/IgM antibodies to Epstein-Barr virus (EBV), viral capsid antigen, early antigen, EBV nuclear antigen and cytomegalovirus (simultaneous detection of immediately early, early, and late antigens). Measurement of an irrelevant antibody for an acute virus infection (i.e., anti-measles virus) will be performed to confirm the specificity of EBV-antibody titer changes. Viral load in blood, saliva, and urine samples will be measured using PCR methodology.

Physiological Stress

Plasma, urinary, and salivary cortisol will be determined before, during, and after bed rest.

FUNCTIONAL STRETCH REFLEX (FSR) TEST

The performance of the major postural muscles (both segmental and central) before, during and after prolonged 6° head down bed rest will be tested by the FSR.

Changes in proprioceptors-mediated sensory-motor reflexes associated with bed rest will be assessed before, during, and after bed rest by measuring changes in the functional stretch reflex. Subjects will remain in the 6° head down supine position with the ankle firmly attached to a dynamometer head in a position of 0 degrees of flexion. Electromyogram (EMG) electrodes will

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then be place on the triceps surae and tibialis anterior muscle groups. A dorsiflexion torque will then be applied at 250°/sec to randomized angular amplitudes of 5, 10, and 15 degrees. Six trials will be conducted at each of the three amplitudes. For half of these trials EMG data on the FSR will be obtained by instructing subjects to resist the force. For the other half, subjects will be instructed to provide no resistance to the torque, enabling collection of T-reflex data. Rectified and filtered EMG data will then be analyzed for both latencies and amplitudes.

GASTROINTESTINAL MOTILITY

Functional and pathologic changes in the GI tract, a site for absorption and bioavailability of drugs and nutrients, will be characterized by the lactulose/acetaminophen (Tylenol®) test.

The characterization of gastrointestinal function and pharmacokinetic changes involves the collection of pre-dose biologic (breath, saliva and urine) samples followed by the ingestion of oral acetaminophen as a pharmaceutical probe, and lactulose, a non-digestible sugar. Saliva, breath, and urine samples will be collected at timed intervals following ingestion of the probes. These tests will require the subject to blow without force, expired breath into a specified bag which will then be returned to the pharmacology laboratory for analysis.

Acetaminophen (Tylenol® syrup, 650 mg,) will be given orally after an initial saliva sample is collected. Saliva samples will be collected for 8 hours after dosing at scheduled intervals. Urine voids will be collected for 24 h post ingestion of test compounds. Samples will then be analyzed for acetaminophen and metabolite concentrations using HPLC (high pressure liquid chromatography). Lactulose, (10 g) which will be given simultaneously with acetaminophen, will be tested using H2 concentrations via collection in to a breath sample bag. Samples will be collected at specified times for 6 h and will be analyzed later that same day.

NASA FLIGHT ANALOGS PROJECT STANDARD MEASURE TESTING SCHEDULE

For all bed rest subjects the study is divided into three phases: a pre-bed rest phase of 13 days for acclimation and baseline data collection, a 90 day bed rest phase, and a post-bed rest recovery phase of 14 days for post-bed rest testing and reconditioning. Each study day is referred to with a conventional naming system. Pre-bed rest days begin at BR-13 and end on BR-1. Days in bed rest begin on BR1. Post-bed rest days begin on BR+0 and subjects are released on BR+13. Subjects stand up briefly on BR60 for planned testing.

Standard Measure	Testing Days Planned			NASA JSC LSRL
	Pre	During	Post	
Neurocognitive Assessment	-12, -10, -8, -5, -3, -1	13, 29, 56, 62	+1, +5	Behavioral Health and Performance
Bone Densitometry (DXA)	-13	62	+2	Bone and Mineral
Peripheral Quantitative Computerized Tomography	-2	62	+2	Bone and Mineral
Clinical Nutritional Assessment	-10, -3	28, 60	+0, +5	Nutritional Biochemistry
Clinical Laboratory Assessment	-10,	28, 60	+0, +5	Clinical
Cycle Ergometry	-12, -7	NA	+0, +11	Exercise Physiology
Isokinetic Testing	-11, -6	NA	+2, +12	Exercise Physiology
Functional Fitness	-10, -5	NA	+3, +13	*ASCR
Functional Neurological Assessment	-10, -4	NA	+0, +1, +2, +4, +7	Neurosciences

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Standard Measure	Testing Days Planned			NASA JSC LSRL
	Pre	During	Post	
Functional Stretch Reflex	-10, -4, -1	5, 20, 59, 90	+0, +3, +5	Neurosciences
Neuroendocrine and Cardiovascular Response to Tilt	-5	NA	+0, +3	Cardiovascular
Plasma volume	-5	3, 21, 31, 60	+0, +3	Cardiovascular
Cardiac Function	-5	7, 21, 31, 49, 60, 75	+0, +3, +13, +30	Cardiovascular
Immune Function Assessment	-10	28, 60	+0, +5	Immunology/Microbiology
Lactulose Breath Hydrogen Test / Acetaminophen Pharmacokinetics	-9	4, 24, 52, 86	+8	Pharmacology

Figure 6. NASA Flight Analogs Project Standard Measure Testing Schedule

*ASCR-Astronaut Strength Conditioning and Rehabilitation Team

5.0 BED REST SUBJECT RECRUITMENT AND SCREENING

The NASA JSC Human Test Subject Facility (HTSF) advertises, recruits and pre-screens candidate subjects to meet unique campaign requirements.

Potential subjects both male and female age 25-55 are pre-screened via telephone interviews by HTSF nurses. Subjects who satisfy the basic inclusion criteria travel to Johnson Space Center for a NASA-modified Air Force Class III physical examination. Subjects are excluded from the study if they: a) are hypertensive, b) have electrocardiogram abnormalities, c) require medication that might interfere with the interpretation of the results (i.e. fluoride, steroids), d) have a recent sub-standard nutritional status, e) have metal implants which could interfere with MRI imaging, f) have a history of thyroid dysfunction, renal stones, mental illness, gastroesophageal reflux, cardiovascular disease, musculoskeletal or sensorimotor dysfunction, or have smoked within six months prior to the start of the study, g) have a personal or family history of thrombosis, h) have a body mass index (BMI) outside of 21-30, i) have abnormal blood or urine chemistries, or j) can not clear a criminal background check. Females must have regular menses, a negative pregnancy test, and not be using hormonal contraceptives. Screening for tuberculosis is also performed.

Blood chemistry testing includes fasting glucose, blood urea nitrogen (BUN), uric acid, creatinine, total bilirubin, aspartate aminotransferase, alanine aminotransferase, alkaline phosphatase, lactate dehydrogenase, glutamyl transferase, sodium, potassium, chloride, phosphorous, calcium, magnesium, CO₂, total protein, cholesterol, triglyceride, high density lipoprotein, low density lipoprotein, and high sensitivity C-reactive protein.

A hematology profile is performed and includes white cell count and differential, red cell count, hemoglobin, hematocrit, ferritin, mean corpuscular volume, mean corpuscular hemoglobin, mean corpuscular hemoglobin concentration, platelet count, red cell distribution width. Urinalysis includes pH, specific gravity, color, appearance, protein, glucose, ketones, blood, bilirubin, urobilinogen, nitrite, and leukocyte esterase.

Following physical screening, subject candidates are tested and interviewed by a psychologist for assessment of their ability to complete all aspects of a study. Psychological screening methods utilize commercial, off-the-shelf psychological tests and International Classification of Diseases (ICD) criteria for psychiatric disorders, derived from current astronaut select-out and select-in procedures. Subjects are also assessed for roommate compatibility.

NASA FLIGHT ANALOGS PROJECT STANDARD SERVICES

After medical and psychological clearance is received study specific screening tests are performed. If more than 30 days has elapsed since initial testing a hematology profile, fasting glucose, sodium, potassium, chloride, CO₂, BUN, creatinine, calcium, and electrocardiogram are repeated before study enrollment.

6.0 FLIGHT ANALOGS RESEARCH UNIT

- Bed rest research facility located at the General Clinical Research Center at the University of Texas Medical Branch
- Maximum capacity of 10 dedicated beds in semiprivate rooms available exclusively for NASA's use
- Common area for subjects to gather and meet with family and visitors
- On site space available to house Standard Measure and research equipment
- Core Laboratory facility with refrigerator, -8° freezer, and centrifuge
- Nursing staff
- Physician services-UTMB attending and medical monitoring (physicians with an out of state license are not eligible for privileges)
- UTMB staff Psychiatrist
- Psychological Support Services
- Reconditioning post study
- Informatics support
 - intra and internet network access
 - telephone services
 - printers and copiers
 - technical support
 - radiology image transfer
- Metabolic kitchen
 - The Metabolic Kitchen is staffed with a research dietician and experienced dietary personnel. They work with the NASA nutritional group to control the total energy and nutrient content of the research subject diets in a manner similar to the control of astronaut in-flight diets. This ensures the collection of comparable and appropriate data.

7.0 SUBJECT SERVICES

- Full time Activities Assistant employed to provide subjects with entertainment, holiday/birthday decorations, arrange group activities, etc.
- Individual subject laptop computer and TV on articulated arms to facilitate viewing.
- Internet access, cable TV, phone card, in room phone with local access.
- Access to movies, music, reading materials.
- Visitation privileges.
- Shower facility with 6 degrees head down tilt capability.

NASA FLIGHT ANALOGS PROJECT STANDARD SERVICES

8.0 FLIGHT ANALOGS PROJECT TEAM RESPONSIBILITIES

- Coordinate investigator meetings
- Coordinate preparation of combined review board packages for the JSC Committee for the Protection of Human Subjects, UTMB Institutional Review Board, and UTMB General Clinical Research Center
- Recruit and perform standard FAP subject screening, reimbursement, and transport
- Provide subject consent briefings
- Provide test subject monitors
- Provide medical monitors and attending physicians
- Develop and manage schedules and the associated logistics to implement integrated studies
- Design and implement Case Report Forms
- Provide a database infrastructure for the collection and storage of data
- Develop data management and sharing plans
- Establish and maintain a bed rest web site to disseminate information.
- Coordinate logistics for shipment of investigator equipment.
- Coordinate storage requirements for investigator equipment.
- Provide a van capable of transporting subjects at 6 degrees head-down for testing at remote locations
- Provide test subject and GCRC medical staff orientations
- Conduct integrated Test Readiness Reviews, safety walk-throughs and operations check-out prior to study start
- Provide on-site coordinators, as required, to support daily testing activities
- Provide a daily operational status report
- Coordinate post study subject follow up testing
- Distribute Standard Measures data to investigators.

9.0 JSC LIFE SCIENCES RESEARCH LABORATORIES (LSRLs)

The Life Sciences Research Laboratories within the Human Adaptation and Countermeasures Division at NASA Johnson Space Center provide the expertise and hold the responsibility for collection and analysis of the FAP Standard Measures data. If a Standard Measure is the same or similar to a flight medical requirement the LSRLs also hold responsibility for collecting those data on crew members before and after spaceflight.

The LSRLs are paid by the Flight Analogs Project to collect these measures on FAP subjects and provide the FAP with the data, which will be shared with the investigators.

10.0 LIFE SCIENCES DATA ARCHIVE

- Ground Analog Database to house standard measure, subject specific, and investigator reduced data
- Archive raw data

NASA FLIGHT ANALOGS PROJECT STANDARD SERVICES

11.0 INVESTIGATOR RESPONSIBILITIES

- Meet with Flight Analogs Project and other investigators to negotiate integrated protocols
- Comply, if possible, with Standard Conditions of Bed Rest
- Accommodate, if possible, collection of Standard Measures of bed rest
- Seek a collaborator within UTMB, if possible
- Prepare their own individual paperwork for the JSC Committee for the Protection of Human Subjects, UTMB Institutional Review Board, UTMB General Clinical Research Center and any individual investigator Institutional Review Boards
- Conduct their individual experiment protocols
- Participate in periodic data debriefs
- Provide their experimental data approximately 2 years after study for inclusion into Flight Analogs database
- Provide manuscript approximately 2 years after study for inclusion into project report

12.0 INVESTIGATOR RESOURCE/FISCAL RESPONSIBILITIES

- The investigator will provide resources for their experiment unique requirements
- The investigator will have responsibility for the costs of any investigator protocol specific screening requirements, equipment, imaging studies, research pharmacy utilization, etc.
- The investigator is responsible for costs associated with personnel for conduct of their own study, travel, and equipment shipping
- The investigator is responsible for test subject travel costs for follow up testing beyond the standard schedule